THE GILGAMESH PROJECT

With multiple awards to his name for cancer research, this childhood prodigy was silenced when his forbidden science began closing in on the secret of eternal life.

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The ability to deal effectively with diseases such as cancer and the consequences of the ageing process remains one of the last major challenges for biomedical science. In order to meet this challenge, it is pivotal that we understand the underlying mechanisms for the cell growth cycle, i.e. why cells grow and divide, why they undergo a process known as differentiation (why and how identical embryonic cells become mature liver, skin, brain cells, etc.) and why, ultimately, cells lapse into senescence and die—causing the metabolic decline and death of the organism.

Problems such as these have obsessed me since childhood and have fired a passionate interest in chemistry and biology long before I enrolled in my first college chemistry course. Considering the extreme human, social and economic costs of diseases such as cancer, heart disease and illnesses associated with advancing age, I could be forgiven for thinking during my high school years that a career devoted to solving these problems was the noblest pursuit possible. If someone had told me that vested interests did *not* want solutions to these most pressing of medical problems, I would have considered them a delusional conspiracy nut. However, my experiences have me permanently disabused of this notion.

In this article, I wish to relate the incredible odyssey that has been my life and some details of the medical research that I have undertaken. I believe that this research, if taken to its logical conclusion, stands a good chance of yielding non-toxic treatments for various forms of cancer and also for prolonging the human life span—possibly indefinitely. Instead of being lauded for these achievements, I have had my education and career in the medical sciences derailed and my life essentially ruined.

There are many lessons to be learned from my experiences that would be worthy of a Hollywood thriller. The first is just how precariously close we stand to bringing the fountain of youth out of the realm of mythology and into the laboratory and ultimately, the clinic—the clues to this endeavour being provided by some of the lowliest (and annoying) organisms on earth. The second lesson is just how committed the medical (and possibly political) establishments are to preventing this from happening and lastly, how deeply the tentacles of vested interests (both personal and institutional) penetrate the hearts and minds of many doctors, administrators and medical educators and function to beat down any type of non-conformist creativity which challenges the status quo.

THE EARLY YEARS

I live in the Midwestern United States where I also grew up and received my education. I currently possess a Bachelor of Science, majoring in biology, and hold a master's degree in political science/international trade. While my classmates in high school were attending ball games and doing what other high schoolers do, I was performing synthetic organic chemistry in a makeshift lab in my home. Developing novel non-toxic agricultural chemicals for the control of pests was my initial preoccupation. Later I became interested in creating non-toxic modalities for the treatment of cancer. These interests were shaped by an unconventional junior high school biology teacher who encouraged *in vivo* experimentation (apologies to anti-vivisectionist readers) and pressed students to do independent research to solve medical problems.

It was during my high school years that I entered and won virtually every science fair with the various projects that I was undertaking. During my senior year, I won first place in my state science fair and received the state medical association's certification of distinction for designing novel classes of antineoplastics (anti-cancer drugs). I was published

professionally, received the American Chemical Society Award, my city's Engineering and Scientific Society award and was inducted into my state's Academy of Science as well as into the New York Academy of Sciences and the American Association for the Advancement of Science before graduating from high school.

In college I continued in my pursuits to unravel the mysteries of how cancer cells develop and metastasise. As it was unusual for undergraduate students to develop and run their own projects, I was fortunate to work with faculty members in my biology and chemistry departments who gave me free run of their facilities. This research led to the development of new classes of compounds which could almost completely block invasion (the process by which cancer cells migrate into healthy tissue). These compounds were essentially non-toxic. I obtained funding for this research through a local oncologist and his hospital, as well as from my university's foundation. My research was featured on local television and in newspapers and I received several accolades, including the Who's Who Among Students in American Universities and Colleges Award. Thus, upon receiving my bachelor's degree I had every reason to suspect a successful passage through medical school and a productive career in medical research.

Upon entering medical school, I again had the fortune of working with a faculty member who understood the potential of my work and gave me any assistance that he could render. I was funded by my oncologist acquaintance as well as through grant money from the American Cancer Society and other government-funded organisations. I became steadily more engrossed in the mysteries of the cell growth cycle and continued synthesising novel classes of cell growth regulators that eventually led me to develop an entirely new perspective on such issues as the human life span, cancer and other illnesses that my medical school professors were presenting as unrelated phenomena. I now present this work in an abbreviated form to facilitate understanding by readers without biomedical backgrounds.

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UNRAVELLING THE MYSTERIES OF THE AGES

Although the stages of the cell growth cycle and the cellular and histological transformations that accompany them are fairly well-known to medical science, the biochemical mechanisms that bring these changes about are poorly defined at best. This is why current therapies for disease states which entail rapid and uncontrolled cell division (such as cancer), consist mainly of poisoning the offending cells with toxic drugs (chemotherapy), radiation (radiotherapy), or removing them through surgery.

Our understanding of the underlying mechanisms for the ageing process leaves even more to be desired. We have virtually no therapies today that can effectively halt or even slow the vaunted biological clock. All we can hope to do is to cover up the signs of ageing through various cosmetic modalities and to treat various age-related maladies (arteriosclerosis, heart disease, etc.,) with therapeutic regimens which address symptoms rather than ultimate causes.

To anyone who has had to care for patients afflicted with the debilitating sequelae of ageing or the horrendous consequences of life-threatening cancers, this is a wholly unsatisfactory state of affairs that cries out for new insights and approaches.

Anyone who identifies the precise factors that regulate what cells do at specific points in the cell growth cycle will have achieved a quantum leap in our understanding not only of the genesis of cancer but also of the age-old question concerning why animals, including humans, age and ultimately die. Such knowledge will not only enable medical science to safely and effectively treat many disease states which today remain enigmatic, but also has profound ramifications for the cosmetic industry.

CURRENT STATE OF LONGEVITY RESEARCH

In order to overcome the limitations of current orthodoxies regarding cell growth and differentiation, it is necessary to briefly review what those orthodoxies are. Within the appropriate body of scholarship dealing with these issues, there have been two basic schools of thought as to what causes cell senescence, cell death and the dysfunctions associated with neoplastic disease (e.g. cancer). The currently dominant one is the free-radical approach.

Reduced to its most basic form, this view holds that cellular dysfunctions, which lead to cancer as well as ageing and eventual cell death, are caused by the destructive action of environmental free radicals upon various important cellular components such as DNA. In this fatalistic view, ageing can be understood as an irreversible and inevitable accumulation of cellular damage. It is my belief that this view is at least partially wrong.

I was once told that research into prolonging the human life span was futile because "every living thing has to grow old and die". Yet, this fatalistic generalisation is patently untrue. Many unicellular organisms are effectively immortal and reproduce by dividing indefinitely, only succumbing to environmental catastrophes—such as the Clorox bleach in your washing machine.

Likewise, there are multicellular organisms for which the concept of growing old is meaningless. Giant sequoia trees can be thousands of years old—yet keep on growing and producing vigorous and functional leaves and internal structures such as xylem and phloem year after year—being felled only by lightning strikes or chain saws. Certain crustaceans such as lobsters grow bigger but do not manifest the age-related declines in reflexes and physiological parameters that plague humans and other animals.

Entomologists have long known that hormonal manipulation can prevent metamorphosis and keep insects in the juvenile state indefinitely. This knowledge has formed the basis for insecticide design.

Likewise, hormonal cues control the development of plants by affecting the proliferation and differentiation of plant cells. Auxin-class herbicides, such as the ubiquitous 2,4-dichlorophenoxyacetic

acid (2,4-D) have been used for eradicating dandelions from lawns for decades. These substances cause discordant cell growth and differentiation which leads to fatal morphological changes and physiological dysfunctions. Considering how important such hormonal systems are to the survival of such a diverse group of organisms, I reasoned that mammals possess systems (even if in a vestigial state) which are functionally analogous, even if the specific chemistry may differ.

A second approach to understanding ageing holds that cell growth, differentiation, ageing and death are *not* the sole result of accumulated cellular damage or of some unstoppable biological clock which resides exclusively within cells, but that these are instead *hormonally* mediated phenomena which result from the interaction of a cell's genes with chemical substances present in the extracellular matrix and produced in remote locations in the body.

This theory is supported by various lines of converging evidence, including research done on the rare disease *progeria*, a syndrome in which various endocrine glands malfunction and the victim rapidly ages and usually dies before the chronological age of twenty.

This devastating and poorly understood disease strongly indicates that the biological clock can be reset and speeded-up, and that this speeding up is associated with the failure of the pineal gland (a pea-sized gland which lies at the centre of the brain), as well as the entire hypothalamic-pituitary axis. The failure of these glands to secrete vital hormones then causes the degenerative changes throughout the body commonly associated with ageing, only much sooner than in healthy individuals who lack the particular genetic defects associated with progeria.

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My own research, both in the library and the laboratory, has led me to gradually put such observations together with findings from other lines of investigation. For instance, it is now acknowledged that the hormone melatonin—secreted by the pineal gland—plays a role not only in the regulation of the sleep-wake cycle, but also in prolonging life span and in some cases, halting and even reversing some of the symptoms of ageing in laboratory animals and humans. The hormone also has anti-cancer activity. Such research, mostly performed in Europe, is amply cited in Dr Walter Pierpaoli's 1995 bestseller *The Melatonin Miracle*, and need not be dealt with in depth here.[1]

Since melatonin is already a commonly sold health supplement, it cannot be patented by pharmaceutical companies and consequently has marshalled little interest from the medical establishment, at least on this side of the Atlantic. However, this is irrelevant from the perspective of my own

I believe that melatonin is an important, but relatively small piece of the overall puzzle and my work has taken this line of research beyond Dr Pierpaoli's discoveries into wholly uncharted territory.

Synthesising this diverse basic research with the results of my own work in cell culture and *in vivo*, I have formulated the following general conclusions:

1. Melatonin's anti-ageing and anti-cancer effects are at least in part due to the fact that this hormone, after it leaves the pineal gland (where it is made), travels to the thymus gland located behind the breastbone and possibly other endocrine glands where it functions as a "releasing hormone" and modulates the synthesis of at least two other chemically distinct hormones unacknowledged by medical science which I will label only as hormone "X" and hormone "Y" for our purposes here. I have identified the chemical structures of these substances.

2. It is both the relative and absolute ambient levels of hormones X and Y in the body that modulate cellular growth, ageing and differentiation phenomena. This effect is in turn probably modulated by melatonin and at least one trace metal or its organometallic complexes. Preliminary indications are that these interactions are complex and remain largely unknown due to the limitations in funds and facilities under which my previous work has been carried out. The production of these substances is probably governed by complex feedback loops that involve the sex hormones, thyroid hormones, etc. Elucidating these relationships must remain one goal for future research.

3. The thymus gland begins the process of involution after the chronological age of 20-30 years in humans. The pineal also calcifies and deteriorates. That is why CT and NMR scans of the heads of older individuals reveal a white pea-sized object in the basal area of the brain which I have seen many people mistake for alien implants. I submit that the deterioration of these glands precipitates a deflection in the concentrations of hormone X, hormone Y, or both. The magnitude and direction (up or down) of these deflections is unknown, but is probably downward.

4. It is this perturbation in the levels of hormones X and/or Y that triggers cell senescence and eventual death, causing tissues to stop turning over and precipitating the physical declines associated with ageing. Since one of these hormones is involved in maintaining cells in a differentiated state, this could provide the long-awaited answer as to why cancer prevalence in general increases as we age, and also why sexual differentiation and other tissue differentiation declines in the same interval.

5. Seemingly intractable problems can only be solved by reinterpreting the problems in novel ways. Cancer cells can be thought of as normal cells which have reverted to a de-differentiated state—i.e. they resemble rapidly dividing, undifferentiated embryonic cells rather than the mature, slowly dividing, properly behaving normal cells of the tissues from which they derive. It is also known to researchers that cancer cells are effectively immortal; if given a proper environment, they can live and reproduce indefinitely, just as can bacteria and certain types of plant and fungal cells. This finding alone indicates that ageing and death are not the inevitable fates that they are made out to be, but are instead the results of a program which can be altered. Although little has been made of this by conventional researchers, it strongly suggests that cancer is not a disease state, but a developmental problem, just as is ageing. Cancer cells are not behaving badly, they are just behaving in a manner inappropriate for their age. It is, in other words, a problem with the biological clock. Since melatonin is one of the substances that modulates the biological clock, this would explain melatonin's anti-cancer effects and also suggested to me that hormones X and Y might have similar effects.

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6. Since the chemical structures of both hormones X and Y are attainable by traditional means of organic synthesis, their manufacture is relatively straightforward. As is also the case with many other currently acknowledged hormones such as the oestrogens and progestins, it is possible to synthesise relatively low molecular weight analogues of hormones X and Y which retain the parent molecule's biological activity. I have prepared several analogues of this type. These compounds show the same cellgrowth altering abilities of the parent molecules although the resources available to me did not facilitate the kind of evaluation necessary to reach detailed conclusions of the precise actions of these compounds.

This leads me to question whether ancient legends of fantastic life span for humans may not have a basis in reality.

7. I have developed other compounds whose chemical structure is quite different from that of either hormones X or Y that seem to have similar effects on cancer cells.

8. The exact mechanism of action of these compounds must at this point remain an object of speculation, since I did not possess the funds or the facilities to properly investigate this issue. Based on the chemical structure of the compounds, however, it is reasonable to assume that, on a cellular level, they act in a manner similar to that of steroid hormones and retinoids (such as vitamin A). This means that they probably penetrate the cell membrane and are then translocated to the nucleus where they either promote or inhibit the expression of genes which regulate the cell growth cycle. This is a much more sophisticated approach and stands in total contradistinction to the mode of action of virtually all existing anti-cancer drugs which are really little more than cellular poisons designed to kill off all rapidly dividing cells. Such a shotgun approach is responsible for the sometimes horrendous side effects associated with conventional chemotherapy.

The compounds that I have developed have obvious application in the non-toxic therapy of cancer and other neoplastic diseases. They also threaten to give medical science completely new insights into the interaction of the ageing process with various disease states. If the melatonin–hormone X–hormone Y axis is indeed responsible for regulating what cells do at particular stages in their life cycle, then we can explain why, for instance, certain cancers tend to occur at particular points in people's lives. As we age, perturbations in the levels of hormones X and Y occur. The hypothesis would predict the incidence of cancer to vary over the span of a person's life as well. Indeed, that is precisely what we observe clinically. As we age, the incidence of various cancers increases. This may be due to the fact that the levels of hormones X and/or Y are no longer sufficient to maintain certain cells in a differentiated state, or that the immune system, whose own cells depend on specific amounts of X and Y, can no longer perform their function of eliminating cancer cells properly.

Finally, although it is too early to be talking seriously about a fountain of youth, I believe that hormones X and Y represent the first steps toward unravelling the mystery of why certain organisms and tissues age. Unlike melatonin, the compounds that I have synthesised represent the first patentable drugs that actually have the potential of reversing or at least slowing the much-dreaded biological clock. They are the first non-steroidal, non-proteinaceous, non-retinoid hormonally active substances other than melatonin and thyroid hormone known to affect cell growth and differentiation in higher animals.

Furthermore, I have discovered that analogues of both hormones X and Y exist in nature and can be prepared, for example, from certain plants. These substances can be incorporated into over-the-counter products such as cosmetics and vitamin preparations without the difficulty of surmounting regulatory hurdles. The impact, for instance, of a wrinkle cream which actually thickens the skin and returns cell turnover rates to levels found in a twenty-year-old should be obvious, especially since today's cosmetic preparations are mainly designed to cover up the effects of ageing.

This leads me to question whether ancient legends of fantastic life span for humans may not have a basis in reality. For example, thousands of years prior to the biblical era, a Sumerian legend relates the tale of a hero-type figure by the name of Gilgamesh who travelled far and wide in his quest for eternal life. He finally found a plant growing under water that was able to bestow the immortality that Gilgamesh sought. As the tale goes, however, instead of consuming the plant, he fell asleep. During his slumber, a snake ate the plant—hence the mythological explanation for snakes constantly shedding and renewing their skin. The moral lesson of the story is, I suppose, "you snooze, you lose". Due to Gilgamesh's carelessness, humankind was denied the secret of eternal life.[2] Alas, mythological descriptions of the "plant," if that is what it was, are not sufficient to make a positive identification.

MEDICAL SCHOOL *REALPOLITIK*

One would have thought that a student capable of doing research such as this would be a cause for great enthusiasm at any medical school. My faculty advisor described me as "the most motivated student he has ever had." Alas, however, I would soon learn that there were individuals who considered me a threat rather than a prodigy, and I was soon to be plunged into a confrontation with forces that, at the time, I could not comprehend.

Between my first and second year of medical school, I was summoned to the office of a school administration official. Conversation quickly turned to my research. This raised my interest, as this official's duties did not include oversight of student research programs. He declined to answer when I asked the identity of the person that had informed him of my work. He asked why I had decided to create my own research project rather than simply signing on to one of the many existing projects offered by faculty members. This was, in his words "what most students did." I answered that I was not "most" students and that I had entered medicine because I wanted to find new solutions to problems that conventional research had failed to find. Rather than eliciting praise and encouragement, my answer only seemed to make him impatient and agitated. He enquired as to what was wrong with the available research projects. I responded that they were mundane and too limited by conventional paradigms to yield anything of importance in our battle with disease. I now went on the offensive and asked what was wrong with *my* research, especially in light of the fact that I was bringing money and positive publicity to the school. He replied that "of course there was nothing wrong", and this concluded our meeting. I could not help but be left with the impression that this official did not accomplish his aims. My inquiries to other students revealed that no one else had undergone such an experience.

This encounter was a turning point in my sojourn through medical school and the subsequent campaign of behind-the-scenes persecution and harassment levelled against me left me thinking that someone was taking lessons from the *Malleus Maleficarum*.

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One day I was summoned to the dean's office and told that there was "something wrong" with my performance in a particular class. Since my grades had been good in this class up till that point, I was taken aback. I asked the dean to tell me precisely what I was doing wrong and who had made the criticism. I also asked why the person making the complaint had taken it to the dean instead of addressing me directly as per school protocol. He refused to answer and became agitated. I replied that if indeed I was doing something wrong I had the right to know the precise nature of the complaint as well as the identity of the person making it. The dean's reply was that I had no such right because his office was not a courtroom. This was to become a fairly standard line of defence for the medical school administration.

Despite my initial good grades and evaluations, the situation deteriorated as I progressed through clinical clerkships. Despite the fact that my performance outshone that of many other students, I found myself receiving negative evaluations. Many of these evaluations were from individuals that I *never* served under, and hence, were pure fabrication. On other evaluation forms, the signature of the evaluator was either absent altogether or was so illegible that even the clerkship coordinator claimed not to know who the person was. This was an obvious attempt to shield the individual from litigation. Protesting this kind of outright fraud to medical school administration fell on deaf ears, and only resulted in new criticism charging that I was being "defensive." In classic witch-hunt fashion, any attempts by me to show that the charges against me were false were only reinterpreted as additional evidence of my guilt or even psychopathology. I was referred to a psychologist and put through a battery of personality inventories. When these came back normal, the school administration simply ignored the results and proceeded to make me jump through an infinite series of new hoops in order to make me appreciate my status as *persona non-grata*. This treatment finally resulted in my leaving medical school partway through my third year. My antagonists realised that I could not afford legal aid and thus felt secure that their machinations could not be effectively countered.

Other more mysterious goings-on seemed to swirl around my research while at medical school. One faculty member refused to address me in the halls and made a point of walking out during conferences when I presented my research. On more than one occasion, I entered my lab to find that my possessions had been searched. To top things off, I received phone calls from someone claiming to be my friend. This person informed me that things would "only get worse" for me at medical school unless I "stopped playing God". He refused to give his name or to explain precisely what he meant by his admonition.

As one can imagine, my leaving medical school was like lifting a huge weight from my shoulders, despite the fact that I had to discontinue my research. The oncologist that I had worked with later perished ostensibly of a heart attack while on vacation.

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Since I cannot show that this was anything but a natural occurrence, I leave it to the reader to decide. After his death, the hospital where he was employed no longer funded my project citing "other priorities".

When all is said and done, what are we to make of all this? Was I the target of industrial espionage? If so, they got nothing, as I have always made a point of carrying my lab notebooks with me at all times and even my faculty advisor was not made privy to the chemical formulas of the compounds that I was developing.

Was this something entirely different? Was it an attempt to simply quash my research? If so, did this involve only officials at the medical school or did it go higher? What could have evoked such a concerted hate campaign against, of all people, a lowly medical student? Did "they" know something about the direction and ramifications of my research that even I did not know at the time?

Given the vitriol directed against me, I cannot help but think that I am on the right track—*to something*. I suppose that I should thank my tormentors for inadvertently confirming what they did not let me have time to confirm in the lab.

If the goal of the powers that be was to marginalise me, then they have succeeded, at least for the time being—I am unemployable and my life has been reduced to financial ruin. I have pursued education in other fields. I am currently attempting to pursue my research privately since it remains patentable. I have made arrangements that all proprietary details of the research be made public in the event of my untimely demise, although I believe that my tormentors have been quite happy keeping me jobless and impoverished.

Since becoming an avid NEXUS reader a couple of years ago, I have interpreted my plight in a different light and have begun to ask questions that would never have occurred to me in medical school. Up until recently, I have operated under the naïve premise that the purpose of the health care industry was to eliminate disease and promote human well being. NEXUS readers know better. I leave readers with the following questions and welcome feedback: What would the implications be for the health care juggernaut if most illnesses associated with advancing age could be eliminated by having everyone take one pill daily? What would happen to our beleaguered social security system if the human life span could be doubled? What would be the impact on organised religion if one of the two certainties of life—i.e. death—was no longer a certainty? ∞

About the Author:

Andrew Sokar is a biologist who lives in the Midwestern US. He has a Bachelor of Science, majoring in biology and a master's degree in political science with a specialisation in internatinal trade, for which he graduated with high distinction. He continues to pursue his research independently, especially into the over-the-counter applications for his rejuvenation technology. He welcomes correspondence at: slowsubversion@yahoo.com.

Endnotes

1. Walter Pierpaoli, William Regelson and Carol Colman, 1995, *The Melatonin Miracle,* Pocket Books, New York. See also William Regelson and Carol Colman, 1996, *The Superhormone Promise,* Pocket Books, New York

2. N.K. Sanders, 1972, *The Epic of Gilgamesh*, Penguin, London